REMARKS

Claims 1-22 are pending. By this submission, claims 17-22 have been canceled and claims 1, 5, 9, and 13 have been amended, without prejudice or disclaimer of any previously claimed subject matter. Thus, claims 1-16 are currently under consideration.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Support for the amendments to the claims may be found, *inter alia*, at page 17, lines 18-20. Accordingly, no new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with Markings to Show Changes Made**."

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance, which is respectfully requested.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-22 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled for a method of reducing the severity of a symptom of papillomavirus infection in any individual or mammal. Applicants respectfully traverse this rejection.

As an initial matter, Applicants respectfully note that claims 1-8 are drawn to a method of delaying development of a symptom of papillomavirus infection and claims 17-22, now canceled, were drawn to kits. These claims do not appear to be encompassed within the scope of an enablement rejection which is directed to claims drawn to a method of reducing the severity of a symptom of papillomavirus infection. Thus, only claims 9-16 appear to be within the scope of this rejection.

The Examiner has stated that the claimed invention is enabled in four different mammalian species, mice, dogs, rabbits, and humans, but that it is not enabled in "any individual or mammal." Solely to expedite prosecution and without prejudice or disclaimer of previously-claimed subject matter, claims 9-16 have been amended to recite a method of reducing severity of a symptom of papillomavirus infection *in a mammal* and thus are no longer drawn to "any individual or mammal." As discussed below, in view of the working examples and disclosure in the specification, enough guidance is provided to enable one of skill in the art to practice the invention as presently claimed without undue experimentation.

The Examiner states that there is a "high degree of uncertainty in the art with regard to extending results obtained in one species to other species" and that "the variability among mammalian species provides a high degree of uncertainty in extending results obtained with mammals to another genus." Office Action, page 4. The claims as amended are drawn only to mammals, rendering the Examiner's statements regarding extension of results to individuals other than mammals moot. Further, Applicants respectfully submit that the possibility that the invention may not work in every species encompassed by a claim does not necessarily render the claim nonenabled, because a claim may encompass inoperative embodiments. MPEP § 2164.08(b). The court in *Atlas Powder Co. v. DuPont*, 750 F.2d 1569, 1576 (Fed. Cir. 1984) stated that "[i]t is not a function of the claims to specifically exclude . . . possible inoperative substances." Further, the MPEP states that "[t]he standard [for enablement] is whether a skilled person could determine which embodiment. . . would be inoperative or operative *with the expenditure of no more effort than is normally required in the art.*" MPEP 2164.08(b) (emphasis added). The Examiner's statement that "[t]he level of skill in the relevant art is very high," (Office Action, page 4) suggests determination of operability of the invention in a particular species would be a matter of routine. Particularly, since the Examiner has conceded that the invention is enabled in *four mammalian species*, a determination of which mammalian species would constitute operative embodiments of the invention as presently claimed would require an

expenditure of effort that is no greater than what is *normally* required using the generally high skill level in this art.

In response to the Examiner's contention that "because there is a high degree of variability in the effectiveness of CpG oligonulceotides at stimulating the immune system of different mammalian species it is not possible to extend these teachings to species other than those for which working examples already exist," (Office Action, page 4), Applicants reiterate their previous arguments that experimental data does not need to be provided for every species encompassed within a claim for the claim to be enabled. Requiring a test with every species covered by a claim in order for the claim to meet the enablement requirement is contrary to the well-established law of enablement, which permits testing for desired and/or operative embodiments (*In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). As discussed in paper no. 13, the working examples that are provided in the specification are well-accepted model systems for the study of papillomavirus infection in mammals, to which the claims as amended are presently directed. As the court recognized in *In re Angstadt*, 537 F.2d 498, 502 (CCPA 1976), it would be a prohibitive burden for the Applicants if they were required to test each species within the scope of their claims in order to satisfy the enablement requirement. Thus, the results in the working examples in the specification with two different mammalian species, coupled with the teaching of the art with regard to two other species, as cited by the Examiner, and the disclosure of how to make and use the invention, is sufficient to enable the currently-pending claims.

Further, the Examiner states that the practice of the invention with species that are not in the working examples or the prior art would require a skilled artisan to perform empirical experimentation, to identify an oligonucleotide sequence that can effectively stimulate the immune system in a particular species or to identify the structural determinants that dictate species specificity of CpG immunomodulation. Applicants respectfully submit that the test for enablement is not whether a certain amount of experimentation is required to practice an invention, but rather whether the amount of experimentation is "undue." As the court held in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988), the test for enablement does not rest merely on the

quantity of experimentation that would be required to practice an invention, "since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Applicants have provided data in the form of working examples that shows that the claimed invention works in two mammalian species that are established model systems for papillomavirus infection. The Examiner concedes that the invention is enabled in at least two other mammalian species, and has provided no evidence that the claimed ISS will not work in other mammalian species. Further, it would be a matter of routine for one of skill in the art to make and test an ISS according to the claims, examples of which are disclosed in the specification (see, for example, page 22, line 19 - page 24, line 13), in different species, to determine which embodiments of the presently-claimed invention (*i.e.*, mammalian species) are operative and which are not. Thus, it would not require undue experimentation to practice the invention in mammals, to which the claims are currently directed.

The court in *In re Wands* found that the enablement requirement was satisfied by a "disclosure [that] provides considerable direction and guidance on how to practice [the] invention and presents working examples," in view of the fact that "[t]here was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *Id.* at 740. With respect to the present invention, the Examiner has admitted that the level of skill in the art is high. Further, the specification provides considerable guidance as to how to practice the invention using well known methods. For example, means of administration (pages 37-39), dosage ranges (page 37), ISS-containing polynucleotides and methods for their synthesis (pages 21-29), administration regimens (pages 34-35), and formulations (page 36) are all provided in the disclosure. The specification also presents working examples, as discussed above. Thus, following the reasoning in the *In re Wands* decision, the disclosure is adequate to enable the invention as currently claimed.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 9-22 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled for a method or composition for reducing severity of a symptom of papillomavirus infection wherein the composition is administered prior to the development of a lesion or outside of the affected area. Claims 17-22 are now canceled, rendering the rejection moot with respect to these claims. Applicants respectfully traverse this rejection.

Applicants herein have discovered that an ISS may be administered alone, *without a papillomavirus antigen*, to reduce the severity of a papillomavirus infection. The Examiner contends that effectiveness of immunostimulation with CpG oligonucleotides is dependent on the proximity of an antigen to the site of administration of the oligonucleotide, and that in the present invention, antigen is provided by the active infection at the site of a papillomavirus lesion. Applicants respectfully submit that the Examiner has provided no evidence that a papillomavirus antigen is required in close proximity to the ISS when it is administered. In an enablement analysis, the burden is on the Examiner to provide relevant evidence as to why a claim is not enabled (MPEP § 2164.04), rather than just a blanket statement, not backed up by evidence of any kind, that antigen must be provided in conjunction with the ISS for the claimed invention to work. Similarly, the Examiner has provided no evidence to support his statement that "antigen is provided by the active infection at the site of the lesion."

Further, the Examiner states that a lack of teaching in the prior art as to the effectiveness of an ISS when administered in the absence of antigen would not lead a skilled artisan to predict that such embodiments of the claimed invention would be operable. Applicants respectfully point out that the test for enablement is whether the disclosure teaches one of skill in the art to make and use the claimed invention without undue experimentation, not whether one of skill in the art would predict that the claimed invention would work based on the teachings of the prior art. One of the bases of the claimed invention is that an ISS may be administered in the absence of antigen to reduce severity of a symptom of papillomavirus infection. As discussed above, the Examiner has provided no evidence that antigen is required.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 102(b)

Claims 17, 18, 21 and 22 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by Dartmann et al., *Virology* (1986) 151:124-130. These claims have been canceled, rendering this rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejections Under 35 U.S.C. § 102(a)

Claims 17-19, 21 and 22 are rejected under 35 U.S.C. 102(a) as allegedly anticipated by Schwartz, WO 99/62923. These claims have been canceled, rendering this rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a).

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882001300.

Respectfully submitted,

Dated: December 19, 2002 By: Jill A. Jacobson

Jill A. Jacobson
Registration No. 40,030

Morrison & Foerster LLP
755 Page Mill Road
Palo Alto, California 94304-1018
Telephone: (650) 813-5876
Facsimile: (650) 494-0792

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 17-22 have been canceled.

Claims 1, 5, 9, and 13 have been amended as follows:

1. (Twice Amended) A method of delaying development of a symptom of papillomavirus infection in [an individual] a mammal who has been exposed to papillomavirus, comprising administering a composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said [individual] mammal, wherein the ISS comprises the sequence 5'-C, G, pyrimidine, pyrimidine, C, G-3', wherein a papillomavirus antigen is not administered in conjunction with administration of said composition, and wherein said composition is administered in an amount sufficient to delay development of a symptom of papillomavirus infection.

5. (Once Amended) The method of claim 1, wherein the [individual] mammal is a [mammal] human.

9. (Once Amended) A method of reducing severity of a symptom of papillomavirus infection in [an individual] a mammal infected with papillomavirus, comprising administering a composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said [individual] mammal, wherein the ISS comprises the sequence 5'-C, G, pyrimidine, pyrimidine, C, G-3', wherein a papillomavirus antigen is not administered in conjunction with administration of said composition, and wherein said composition is administered in an amount sufficient to reduce severity of a symptom of papillomavirus infection.

13. (Once Amended) The method of claim 9, wherein the[individual] mammal is a [mammal] human.